PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)* see form PCT/ISA/210 (second sheet)	
Applicant's or agent's file reference see form PCT/ISA/220	**FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US2005/000024	21.01.2005	03.02.2004

International Patent Classification (IPC) or both national classification and IPC
C07D403/04, C07D409/04, A61K31/4184, A61P35/00

Applicant
ELI LILLY AND COMPANY

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:	Authorized Officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Lauro, P Telephone No. +49 89 2399-8288

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US2005/000024

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US2005/000024

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	
	No:	Claims	1-7
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-7
Industrial applicability (IA)	Yes:	Claims	1-7
	No:	Claims	

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43*bis*.1 and 70.10)

and / or

2. Non-written disclosures (Rules 43*bis*.1 and 70.9)

see form 210

Re Item V.

1. Reference is made to the following documents:

D1 : DATABASE CA [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; KAI, YASUNOBU ET AL: "Preparation of pyrazole derivatives as antiviral agents" XP002328394 retrieved from STN Database accession no. 1996:607249

D2 : WO 03/042211 A (SMITHKLINE BEECHAM CORPORATION; GASTER, LARAMIE, MARY; HARLING, JOHN,) 22 May 2003 (2003-05-22)

D3: WO 02/072576 A (PFIZER PRODUCTS INC; DOMBROSKI, MARK, ANTHONY; LETAVIC, MICHAEL, ANTHO) 19 September 2002 (2002-09-19)

D4: WO 97/25045 A (SMITHKLINE BEECHAM CORPORATION; ADAMS, JERRY, L; BOEHM, JEFFREY, C; LE) 17 July 1997 (1997-07-17)

D5: WO 2004/014900 A (ELI LILLY AND COMPANY; BONJOUKLIAN, ROSANNE; DE DIEGO GOMEZ, JOSE, EUG) 19 February 2004 (2004-02-19)

2. Document D5, which was published after the priority date of the current application is not taken into account for the present opinion.

3. **Novelty**

The compounds of the present application are anticipated by D1, which exemplifies several compounds which fall under the definition of formula (I) as claimed in claim 1. D2 describes in Example 18 a compound which falls under formula (I) of the present application. Novelty is not acknowledged re D1 and D2.

4. **Inventive step**

The problem underlying the current application resides in the provision of benzimidazole or benzotriazole characterized by a 5-heterocyclic ring attached to the benzo ring of the benzimidazole moiety as kinase inhibitors.

Kinase inhibitors are disclosed in D2 to D4. The general formula of D2 comprises the compounds of formula (I) of the present application and specifically an example (see example 18) is given which falls within the subject-matter of the present application.

Moreover, D3 discloses benzimidazole derivatives substituted by 5-heterocyclic rings, which only differ from the compounds of the present application in the presence of an oxo group in position 2 of the benzimidazole. In addition D4 generically discloses that imidazole attached to a benzimidazole are suitable as kinase inhibitors. The prior art is therefore considered to contain all information to arrive at the compounds of the present application with the expectation that they would possess kinase inhibitory activity. In the absence of experimental data which show unexpected effects for the compounds of the present application compared to the structurally closest compounds of the prior art, inventive step cannot be acknowledged.